

**UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF OHIO
EASTERN DIVISION**

**IN RE NATIONAL PRESCRIPTION
OPIATE LITIGATION**

This document relates to:

Track Three Cases

**MDL No. 2804
Case No. 17-md-2804
Judge Dan Aaron Polster**

**DECLARATION OF STEVEN N. HERMAN IN SUPPORT OF THE PHARMACY
DEFENDANTS' MOTION TO EXCLUDE CERTAIN OPINIONS
AND TESTIMONY OF DR. KATHERINE KEYES**

EXHIBIT 17

Physicians' Behavior and Their Interactions With Drug Companies

A Controlled Study of Physicians Who Requested Additions to a Hospital Drug Formulary

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Objective.—It is controversial whether physicians' interactions with drug companies affect their behavior. To test the null hypothesis, that such interactions are not associated with physician behavior, we studied one behavior: requesting that a drug be added to a hospital formulary.

Design.—Nested case-control study.

Setting.—University hospital.

Participants.—Full-time attending physicians. Case physicians were all 40 physicians who requested a formulary addition from January 1989 through October 1990. Control physicians were 80 randomly selected physicians who had not made requests.

Main Exposure Measure.—Physician interactions with drug companies, as determined by survey of physicians (response rate, 88% [105/120]).

Results.—Physicians who had requested that drugs be added to the formulary interacted with drug companies more often than other physicians; for example, they were more likely to have accepted money from companies to attend or speak at educational symposia or to perform research (odds ratio [OR], 5.1; 95% confidence interval [CI], 2.0 to 13.2). Furthermore, physicians were more likely than other physicians to have requested that drugs manufactured by specific companies be added to the formulary if they had met with pharmaceutical representatives from those companies (OR, 13.2; 95% CI, 4.8 to 36.3) or had accepted money from those companies (OR, 19.2; 95% CI, 2.3 to 156.9). These associations were consistent in multivariable analyses controlling for potentially confounding factors. Moreover, physicians were more likely to have requested formulary additions made by the companies whose pharmaceutical representatives they had met (OR, 4.9; 95% CI, 3.2 to 7.4) or from whom they had accepted money (OR, 1.7; 95% CI, 1.0 to 2.7) than they were to have requested drugs made by other companies.

Conclusion.—Requests by physicians that drugs be added to a hospital formulary were strongly and specifically associated with the physicians' interactions with the companies manufacturing the drugs.

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PHYSICIANS interact with drug companies in many ways, but these interactions are controversial.¹⁻¹¹ For example, according to the American Federation for Clinical Research, "[I]ndustry-sponsored lectureships, symposia, and support for research are an integral part of the biomedical research and educational system that would be severely damaged by disallowing such

activities."¹² In contrast, some see in such arrangements "the essence of good bribery."¹¹ This controversy is due, in part, to the paucity of studies of physicians' behavior and factors that affect it.

Many types of physician behavior relate to drugs. Not only do physicians prescribe the drugs that patients buy, but physicians who speak about drugs at medical symposia may influence their listeners' prescribing behavior,⁵ faculty physicians shape the prescribing behavior of their students, and physicians' research affects the availability of and indications for drugs. An additional physician behavior—requesting that a drug be added to a hospital formulary—is also important to drug sales,¹³ because the formulary regulates the drugs available for physicians to prescribe for hospital patients. Furthermore, in teaching hospitals, the formulary determines which drugs are most easily prescribed by physicians in training, who are developing prescribing styles likely to persist in their careers.

Physicians generally perceive their behavior regarding prescription drugs as motivated mainly by drug performance data, yet their beliefs about selected drugs more closely matched advertising claims.¹⁴ Although the influence of drug companies on physician behavior has not been extensively studied, available evidence suggests that physician behavior with respect to drugs may be associated with drug company promotional activities.¹⁵⁻¹⁹ Most studies have been limited, however, in that they relied solely on physicians' reports of their own behavior rather than observing it directly and did not relate the behavior of individual doctors to their interactions with specific companies.

STUDY GOAL AND HYPOTHESES

Our goal was to determine if physicians' interactions with drug companies were associated with a physician behavior that was independently observed, namely, requesting that a drug be added to our hospital formulary. To accomplish this goal, we compared two groups of physicians, physicians who had requested that drugs be added to a hospital formulary and other physicians who had not. We studied interactions between doctors and drug companies in general and between doctors and the specific companies manufacturing drugs that had been requested. For each interaction, we tested the null hypothesis, that interactions were not associated with the behavior. In particular, we tested three discrete null hypotheses: (1) Physicians who interacted with drug companies in general were no more likely than other physicians to have made formulary requests; (2) physicians who interacted with specific companies were no more likely than other physicians to have requested drugs manufactured by those companies; and (3) physicians who interacted with specific companies were no more likely to have requested drugs manufactured by those companies than drugs manufactured by other companies.

METHODS

Setting

The study was conducted at the University Hospitals of Cleveland (Ohio), an 874-bed teaching hospital affiliated with Case Western Reserve University School of Medicine. A request for the addition of a drug to the formulary may be made by any health care professional at the hospital who completes a standard form about the drug's pharmacologic properties. The form stipulates that requests may not be made for drugs if the requester is involved in research on the requested drug that is sponsored by the company making the drug. All forms are included in the minutes of the Formulary Review Subcommittee of the Pharmacy and Therapeutics Committee.

During the period of this study, pharmaceutical sales representatives were permitted access to most patient care areas, except the emergency department, nurseries, and intensive care, labor, delivery, operating, recovery, and dialysis units. Institutional review board approval was obtained for this investigation.

Subjects

The study had a nested case-control design. Subjects were physicians on the full-time attending staff at University Hospitals of Cleveland. Case physicians,

who were identified by review of the minutes of the Formulary Review Subcommittee of the Pharmacy and Therapeutics Committee, were all 40 physicians who had requested that a drug be added to the formulary from January 1, 1989 to October 31, 1990; all requests during that time period had been made by full-time attending physicians. Control physicians were those who had not made formulary requests and were members of departments directly involved in selecting medications for patients; physicians in the departments of pathology, nuclear medicine, diagnostic radiology, and radiation therapy were excluded. Eighty control physicians were selected randomly from the 330 eligible physicians to avoid overmatching.²⁰

Data Collection and Measures

Drugs.—There were 55 requests for 52 commercially available drugs to be added to the hospital formulary; 28 physicians requested that one drug be added, 10 requested two drugs, one requested three drugs, and one requested four drugs. The company manufacturing the drug at the time of the request or the company specifically noted by the requesting physician (if more than one company manufactured the drug) was considered to be the manufacturing company. There were 35 manufacturing companies.

The requested drugs were classified by a doctor of pharmacy who was familiar with the University Hospitals formulary but not associated with this study, using a modification of the Food and Drug Administration therapeutic rating.²¹ The requested drugs were classified as representing a major therapeutic advantage over therapies existing in the formulary (n=13), a modest advantage (n=13), or little or no advantage (n=29); this classification was specific to the formulary (Table 1). The drugs were also classified as having been requested for addition to the formulary in the year following Food and Drug Administration approval (n=23) or after that year (n=23) (this information was not available for one drug).

Demographic Characteristics and Publications of Physicians.—Demographic information about all physicians was obtained from the hospital staff office, the medical school, and the *Compendium of Medical Specialists*.²² MEDLINE-indexed publications by each physician in 1989 were classified as reflecting laboratory-based or patient-based research.

Survey Instrument.—To measure interactions with drug companies, a survey instrument was developed, to be completed by all physicians. This instru-

Table 1.—Drugs for Which Requests Were Submitted for Addition to a Hospital Formulary, Classified According to Their Therapeutic Advantage Over Drugs Already in the Formulary*

Major Advantage

Clofazimine
Clozapine
Epoetin alfa
Fluconazole
Flurbiprofen sodium ophthalmic drops
Ganciclovir
Levamisole
Mefloquine
Methoxsalen
Nimodipine
Octreotide
Pulmonary surfactant, synthetic
Typhoid vaccine, oral

Modest Advantage

Adenosine
Bupropion
Carboplatin
Flutamide
Ifosfamide/mesna
Ketorolac tromethamine
Moricizine
Nafarelin acetate
Omeprazole
Pergolide mesylate
Permethrin 1%
Permethrin 5%
Selegiline hydrochloride

Little or No Advantage

Albuterol Repetabs
Albuterol Rotacaps
Acebutolol hydrochloride†
Cefixime
Ciclopirox†
Dezocine
Diclofenac
Diltiazem hydrochloride sustained release
Disopyramide
Esmolol concentrate
Estradiol, transdermal
Flecainide acetate
Goserelin acetate
Hydroxypropyl methylcellulose drops
Lidocaine spray
Lisinopril
Magnesium gluconate
Methotrexate Dosepack
Multivitamins, renal
Oxycodone with aspirin
Nifedipine extended release
Pancrelipase
Propafenone hydrochloride
Propofol
Scopolamine, transdermal
Ticarcillin/potassium clavulanate†

*Drugs in bold type were not accepted for addition to formulary.

†Drugs for which two requests were submitted.

ment was pretested by seven physicians to determine ambiguous items and was revised accordingly; the format of specific questions is available on request.

The instrument inquired about the number of patients cared for by each physician. It also inquired about four types of interactions with drug companies in the past year: traditional detailing by pharmaceutical company representatives, acceptance of money from drug companies to support attendance at educational symposia, acceptance of money to speak at educational symposia, and acceptance of money for research.

Each physician was asked about these interactions with drug companies in gen-

Table 2.—Physician Interactions in the Past Year With Drug Companies in General, According to Self-reports by Physicians Who Submitted Formulary Requests (Cases) and by Those Who Did Not (Controls)

Type of Interaction*	No. (%) of Cases (Physicians Submitting Requests) (n=36)†	No. (%) of Controls (Physicians Not Submitting Requests) (n=69)†	P
Shared meals worth > \$10			
Never	17 (47)	42 (61)	.01
Rarely	11 (31)	24 (35)	
Occasionally	3 (8)	2 (3)	
Often	5 (14)	1 (1)	
Accepted money for travel or lodging to attend educational symposia			
Never	27 (75)	63 (91)	.06
Rarely	7 (19)	5 (7)	
Occasionally	2 (6)	0 (0)	
Often	0 (0)	1 (1)	
Accepted money to speak at educational symposia			
Never	17 (47)	55 (80)	<.001
Rarely	5 (14)	9 (13)	
Occasionally	5 (14)	4 (6)	
Often	9 (25)	1 (1)	
Accepted money to perform research			
No	14 (39)	49 (71)	.002
Yes	22 (61)	20 (29)	

*Types of interactions are defined in the text. "Rarely" was defined as one to two times in the past year, "occasionally" as three to five times in the past year, and "often" as more than five times in the past year. One column does not total 100% due to rounding.

†Of the 120 physicians, 36 cases and 69 controls responded to the survey instrument.

eral and with seven specific drug companies. The 35 companies whose drugs had been requested were randomly divided into groups of seven companies each. Each case physician was asked about the group containing the company or companies whose drugs he or she had requested. For each case physician two unmatched control physicians were asked about interactions with the same seven companies.

Case and control physicians were sent the survey instrument with a letter asking them to participate in a study of drug companies' interactions with physicians; the study hypotheses were not specified in the letter. Physicians were informed that all answers would be coded and kept confidential.

Survey data were available for 105 (88%) of 120 physicians: 36 (90%) of 40 case physicians, who had requested 47 (85%) of the 55 drugs, and 69 (86%) of 80 control physicians. Of the 36 cases on whom survey data were available, 26 had requested that one drug be added, nine had requested two drugs, and one had requested three drugs. For specific companies, this response rate permitted comparison of 47 potential interactions between case physicians and the specific companies whose drugs they had requested and 82 potential interactions between the unmatched control physicians randomly assigned to each case and the same companies.

Independent Information About Drug Company-Sponsored Research.—Physician responses about participation in

research sponsored by drug companies were validated by data from hospital departments about such research in 1989 and 1990. This information was provided for 92 (77%) of the 120 physicians. In every instance in which departmental information indicated that a physician who had completed the survey had performed drug company-sponsored research, the physician had provided this information in the survey.

Analytic Strategy

The overall strategy for analysis was to test each of the three specific null hypotheses by determining associations between the physician behavior (requesting that a drug be added to the hospital formulary) and types of physicians' interactions with drug companies, and then to examine any observed associations for consistency.

The first hypothesis was tested by examining associations between requesting a formulary addition and physician interactions with drug companies in general (data available on 36 cases and 69 controls from the completed survey instruments).

The second hypothesis was tested by examining associations between requesting a formulary addition and physician interactions with specific drug companies. The rates of interaction of case physicians with each specific company whose drug the case physician had requested (n=47) were compared with the rates of interaction of the randomly assigned control physicians asked about

the same specific companies (n=82). Multivariable logistic regression models²³ were used to determine whether any observed associations were confounded by other physician characteristics. Although this analysis used unmatched controls,²⁰ the consistency of these results was examined with an alternative analysis comparing case physicians and physicians matched for types of patients seen. In this analysis, for each potential interaction between a case physician and the company making the drug he or she had requested (n=47), a matched comparison physician was selected who had not requested a drug made by that company but who had been surveyed about interactions with that company. Matching of physicians in this way by type of patient seen was possible for 32 of the 47 formulary requests; in 21 the physicians were in the same department, and for the remaining 11 requests the physicians were in different departments but cared for patients with similar problems (for example, a rheumatologist was matched to an orthopedic surgeon). Of the 32 matched comparison physicians, 24 were control physicians and eight were case physicians who had not requested drugs made by the manufacturer of the drug requested by the case to whom they were matched. The comparison involved a matched analysis in which the odds ratio was calculated as the ratio of discordant pairs.²⁰

The third hypothesis was also tested by examining associations between requesting a formulary addition and physician interactions with specific drug companies; for this analysis, case physicians were studied with respect to their interactions with the specific companies making the drugs they had requested, compared with their interactions with other specific companies. This comparison also involved a matched analysis in which the odds ratio was calculated as the ratio of discordant pairs.²⁰

Data analyses were conducted using SAS (Statistical Analysis System, Version 6).²³ Associations between dichotomous variables were evaluated by Fisher's Exact Test. Associations between other categorical variables were tested by the χ^2 statistic, with the modification for linear trend when appropriate. Continuous variables in two groups were compared by the Wilcoxon Rank-Sum Test.

RESULTS

Demographic and Professional Characteristics

Case and control physicians were similar in age, academic rank, tenure status, and mean numbers of laboratory- and

Table 3.—Rates of Interaction With Specific Drug Companies Reported by Physicians Who Submitted Formulary Requests (Cases) and Those Who Did Not (Controls)

Type of Interaction*	Interaction Rates, %,† Between		P	Odds Ratio (95% Confidence Interval)
	Cases and Specific Company Manufacturing the Drug Requested (n=47)	Controls and Specific Companies (n=82)		
Met with pharmaceutical representatives	51 (24/47)	7 (6/82)	<.001	13.2 (4.8-36.3)
Accepted money to attend symposia	4 (2/47)‡	0 (0/82)	.13	9.1 (0.4-192.9)§
Accepted money to speak at symposia	11 (5/47)‡	0 (0/82)	<.01	21.4 (1.2-395.4)§
Accepted money to perform company-sponsored research	11 (5/47)‡	1 (1/82)	.02	9.6 (1.1-85.2)
Accepted money to attend symposia, speak at symposia, or perform research	19 (9/47)‡	1 (1/82)	<.001	19.2 (2.3-156.9)

*The types of interactions are defined in the text.

†For each type of interaction with specific companies, responses were available on 47 potential interactions between case physicians and the companies making the 47 drugs they had requested and 82 potential interactions between the randomly selected control physicians assigned to each case and the same specific companies. For cases, the numerator was the number of case physicians who responded that they had experienced a given type of interaction with that specific company, and the denominator was the total number of case physicians responding about interactions with the specific companies making the drugs they had requested (n=47). For controls, the numerator was the number of controls who responded that they had had that type of interaction with the specific company making the drug requested by the case to which the control physician had been assigned, and the denominator was the total number of controls responding about that type of interaction with the specific companies (n=82). These comparisons used a physician's response to a question about an interaction with a company as the unit of analysis. When parallel analyses were performed using data comparing the 47 potential interactions of cases and the specific companies whose drugs they had requested with all potential interactions between controls and specific companies (n=483, since 69 controls were each asked about seven specific companies), the results were consistent.

‡The numerator represents different physicians, not the same physician responding to questions about different formulary requests he or she had made.

§Odds ratios were calculated by the method of Fleiss²⁴ for situations in which one of the observations is zero.

Table 4.—Results of Five Multivariable Models of Cases' and Controls' Interactions With Specific Drug Companies*

Type of Interaction†	Odds Ratio (95% Confidence Interval) for Submitting a Formulary Request for a Drug Made by the Specific Company‡	P
Met with pharmaceutical representatives	3.4 (1.8-6.6)	<.001
Accepted money to attend symposia	7.9 (1.1-55.6)	.04
Accepted money to speak at symposia	3.9 (1.2-12.7)	.03
Accepted money to perform company-sponsored research	9.5 (2.6-35.7)	<.001
Accepted money to attend symposia, speak at symposia, or perform research	5.7 (2.2-14.7)	<.001

*The comparisons used data for the 47 potential interactions of case physicians and the specific companies whose drugs they had requested and the 483 potential interactions between control physicians and specific companies (69 controls were each asked about seven specific companies). Each model included four potentially confounding factors: physician age, gender, appointment in the department of medicine, and number of patients cared for per week. When parallel analyses were performed using only the 82 potential interactions of controls assigned to each case with specific companies as the unit of analysis (Table 3), the results were consistent, except that the analyses for attending and speaking at symposia could not be done because none of the controls had interacted in that way (see Table 3).

†The types of specific interactions are defined in the text.

‡When the interaction rate of each company with controls was also included in each model (because companies' interaction rates differed greatly, from 0% to 60% for meeting with pharmaceutical representatives, for example), the odds ratios were 10.8 (4.4, 26.3), 20.4 (1.8, 250.0), 5.2 (1.5, 18.5), 13.0 (3.1, 52.6), and 7.4 (2.7, 20.4), respectively.

patient-based publications indexed in MEDLINE in 1989. Case physicians, however, were more likely to be male (34 [85%] of 40 vs 53 [66%] of 80; $P=.03$), in the department of medicine (18 [45%] of 40 vs 20 [25%] of 80; $P=.04$), and reported to be caring for more patients per week on average (median, 44 vs 31, respectively; $P=.01$).

Physician Interactions With Drug Companies in General

Most physicians (85 [81%] of 105) met with pharmaceutical representatives. Case and control physicians did not differ in the frequency of their exposure to

many sorts of detailing activities sponsored by drug companies in general, but case physicians reported sharing meals worth more than \$10 paid for by drug companies more often than did control physicians (Table 2).

Case physicians were somewhat more likely ($P=.06$) than control physicians to have accepted money from drug companies to pay for their personal travel or lodging to attend educational symposia, and they were much more likely than control physicians ($P<.001$) to have accepted money to speak at such symposia (Table 2). For physicians who rarely, occasionally, or often accepted money

from drug companies to speak, the odds ratios (with 95% confidence intervals [CIs]) for submitting a formulary request were 1.8 (0.5 to 6.1), 4.0 (1.0 to 16.8), and 29.1 (3.4 to 246.6), respectively, compared with physicians who had never accepted money from drug companies to speak. Cases were also much more likely than controls to have performed research sponsored by drug companies: seven (70%) of 10 cases who submitted two or more requests had performed such research, compared with 15 (58%) of 26 cases who had submitted only one request and 20 (29%) of 69 controls ($P=.001$).

Physician Interactions With Specific Drug Companies: Comparisons of Case and Other Physicians

Physicians who had a variety of interactions with specific companies were more likely than other physicians to have requested that drugs manufactured by those companies be added to the formulary (Table 3²⁴): odds ratios for requesting a drug made by a specific company were 13.2 ($P<.001$), 21.4 ($P<.01$), and 9.6 ($P=.02$), respectively, for physicians who met with pharmaceutical representatives from that company, accepted money from that company to speak at symposia, or accepted money from that company to perform research. Too few physicians accepted money from specific companies to attend symposia to achieve statistical significance. Physicians who accepted money from specific companies for any of the above educational or research activities were much more likely than other physicians to have requested that drugs manufactured by those companies be added to the formulary (odds ratio, 19.2; $P<.001$).

All nine case physicians and the one control physician who had accepted money for educational or research purposes from the companies making the drug requested also had met with pharmaceutical representatives from those companies. Thus, compared with physicians who neither met with representatives nor accepted money from the specific companies, the odds ratios for requesting that that company's drug be added to the formulary were 9.9 (95% CI, 3.3 to 30.2) for physicians who met with representatives from the company but did not accept money and 29.7 (95% CI, 3.6 to 247.3) for physicians who both accepted money and met with representatives from the company.

In five multivariable logistic regression models controlling for four physician characteristics (age, gender, appointment in the department of medicine, and number of patients seen per

Table 5.—Matched Analysis of Potential Interactions of Case Physicians With Companies Manufacturing the Drug Requested and With Other Pharmaceutical Companies

Type of Interaction*	No. of Concordant Pairs†		No. of Discordant Pairs‡		Odds Ratio§ (95% Confidence Interval)
	Case Physicians Interacted With Both Companies	Case Physicians Interacted With Neither Company	Case Physicians Interacted Only With the Company Making Drug Requested	Case Physicians Interacted Only With Other Companies	
Met with pharmaceutical representatives	34	101	102	21	4.9 (3.2-7.4)
Accepted money to attend symposia	1	241	11	5	2.2 (0.8-6.2)
Accepted money to speak at symposia	2	218	26	12	2.2 (1.1-4.2)
Accepted money to perform company-sponsored research	2	218	23	15	1.5 (0.8-2.9)
Accepted money to attend symposia, speak at symposia, or perform research	6	185	42	25	1.7 (1.0-2.7)

*The types of specific interactions are defined in the text.

†For each of the 26 case physicians submitting the one formulary request, there were six possible pairs (one specific company making the drug and six specific companies not making the drug); for each of the nine case physicians submitting two requests, there were 10 possible pairs (two specific companies making the drugs and five specific companies not making the drug); and for the case physician submitting three requests, there were 12 possible pairs (three specific companies making the drug and four specific companies not making the drug).

‡The odds ratio was calculated as the ratio of discordant pairs.²⁰ The numerator was the number of instances (pairs) in which a case physician interacted with the company making the drug requested but not with other specific companies not making the drug. The denominator was the number of instances in which a case physician did not interact with the company making the drug requested but did interact with another specific company not making the drug.

week), each type of interaction with the drug companies making the drugs requested was independently associated ($P < .05$) with submission of a formulary request (Table 4).

Case physicians who had met with pharmaceutical representatives from specific companies were more likely than matched comparison physicians to have requested that drugs manufactured by those companies be added to the formulary (odds ratio, 8.0 [95% CI, 1.4 to 45.9]). For accepting money from specific companies to attend symposia, speak at symposia, or perform research, the odds (95% CI) of requesting a drug made by those companies were 5.0 (0.5 to 46.5), 2.0 (0.4 to 10.6), and 9.0 (1.0 to 77.5), respectively, compared with matched comparison physicians.

Physician Interactions With Specific Drug Companies: Comparisons Among Case Physicians

Physicians who had met with pharmaceutical representatives from specific companies or who had accepted money from specific companies to attend symposia, speak at symposia, or perform research were more likely to have requested drugs manufactured by those companies than they were to have requested drugs manufactured by other companies (Table 5).

Similar proportions of case physicians requested a drug of major or moderate therapeutic advantage (as opposed to little or no therapeutic advantage) when they accepted funding from the drug companies manufacturing the drugs or met with the company's representatives without accepting funding (40% and 44%, respectively) as when they did not accept funding from the companies or meet

with the company's representatives (52%; $P = .8$). More cases requested a drug approved by the Food and Drug Administration in the past year (as opposed to longer than a year) when they accepted funding from the manufacturer than when they met with the manufacturer's representative without accepting funding or when they neither accepted funding nor met with the representative (89% compared with 40% and 41%, respectively; $P = .03$).

COMMENT

These results demonstrate a strong association between a physician behavior, requesting that a drug be added to a hospital formulary, and the doctors' interactions with drug companies. Four aspects of this association deserve emphasis.

First, the association was *strong*: depending on the type of interaction, physicians who interacted with drug companies were from nine to 21 times more likely than other physicians to have requested a drug made by the company with whom they had interacted.

Second, the association was *consistent* for many types of physician-company interactions, including sharing meals paid for by companies, meeting with detailing representatives of the companies making the drugs requested, and accepting money from companies for educational or research activities.

Third, the association was *specific*: physicians who had interacted with specific companies were more likely to request drugs made by those companies than they were drugs made by other companies, and than were physicians who had not interacted with those companies.

Fourth, the association was *independent* of many confounding factors: in matched and multivariable analyses accounting for physician and practice characteristics, the association remained consistent.

Comparison With Past Studies

Past work has suggested that physicians' behavior is associated with and may be affected by their interactions with drug companies. Information presented by 11 physicians at company-sponsored symposia was biased in the company's favor,¹⁹ and some physicians have reported changing their practice after discussions with pharmaceutical representatives or attending symposia.^{16,17} Promotional attributes of published company-sponsored symposia have been demonstrated.²⁵ Also, in-hospital use of two drugs increased after physicians were invited to attend symposia sponsored by the manufacturing companies.¹⁸ Results of the present study are consistent with and amplify those of the past because it avoided many of their limitations. It examined an observed physician behavior in a large, representative sample and quantitatively related the behavior to physicians' reports of their interactions with specific companies.

Limitations

Physician participation in company-sponsored research was validated with departmental data, but measurement of other physician interactions with drug companies relied on the doctors' reports. While some doctors may underreport these interactions, it is unlikely that controls would systematically underreport compared with cases, and thus it is likely that the observed associations are at-

tributable to actual differences between case and control physicians.

The generalizability of these findings to other physicians, nonacademic sites, and other behaviors (such as prescribing) has not been established.

This study does not prove that interactions with drug companies influenced the behavior of the interacting physician; alternative explanations are possible. The temporal direction may have been reversed—ie, physicians, by virtue of their expertise or interest, may have first requested that drugs be added to the formulary and then interacted with the companies whose drugs they had requested. Or, unknown confounding factors may have contributed to our findings. Neither of these alternative explanations is likely, however, given the fact that most of the requested drugs represented little or no therapeutic advantage over drugs already in the formulary and given the strength, consistency, and specificity of the association in univariate, multivariable, and matched analyses.

Many factors undoubtedly influence a

physician's decision to request that a drug be added to a hospital formulary,²⁶ and this study focused on one possible element, interactions between the physician and the company manufacturing the drug. The fact that most formulary requests were not related to certain types of physician interactions with companies—in the majority of requests, physicians had not participated in educational activities or research sponsored by the companies—is completely consistent with an examination of simply one facet of many that may affect complex decisions physicians make about drugs.

These results do not demonstrate physician behavior that is inappropriate, nor do they specifically address the educational value for physicians or benefit to patients of physician-company interactions. The effect of interactions in this study did not appear to be primarily educational, however, since the number and type of interactions between physicians and specific drug companies making the drugs they had requested were unrelated to the therapeutic merits of the drugs.

CONCLUSION

This controlled study of one physician behavior demonstrated a strong and specific association between the behavior and the physicians' interactions with drug companies, independent of the merits of the companies' products.

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